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# ERYTHEMA NODOSUM.

## A REVIEW OF ONE HUNDRED AND FIFTEEN CASES.

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### Association with Tuberculosis.

Wallgren (1938) observed 34 children who had intracutaneous tuberculin tests which were negative before they were taken ill with erythema nodosum. They all became tuberculin positive. Perry (1944) found that 72% of 67 cases of erythema nodosum among children under 15 years of age marked the onset of primary tuberculosis. But the diagnosis was of probable tuberculosis in 29%, based only on positive Mantoux reactions. Doxiadis (1949) recorded that out of 100 children aged up to 14 years with erythema nodosum, 88 had positive tuberculin reactions. In 59 of these, there was an active tuberculous lesion. In none of the children was there any connection between erythema nodosum and rheumatic fever. Special investigations were not made on the 12 tuberculin negative cases but a sore throat or scarlet fever preceded the eruption in six.

In a period of 27 years, Booth (1953) noted 107 cases of erythema nodosum. All the patients except one were under 14 years of age. Forty-four cases had positive tuberculin reactions initially and she said these fell into the group of tuberculous erythema nodosum. But again a positive Mantoux alone was hardly sufficient evidence for this diagnosis. In another 11 cases the Mantoux reaction changed from negative to positive within six months of first being seen. Of these two groups, 33 cases had radiographic evidence of tuberculosis. Booth wrote that in this series there was a high incidence of children with a positive tuberculin test compared with a low incidence of children with positive tuberculin tests in the average population. The same author admitted that erythema nodosum could occur rarely in association with rheumatic fever and suggested that streptococcal infection was the exciting factor in a predisposed individual. Fry (1952) also stressed the rarity of erythema nodosum in rheumatic fever.

Verney (1955) investigating the incidence of tuberculosis in university stu-

dents and student nurses found that of 11 cases of erythema nodosum 7 developed pulmonary tuberculosis and 1 contracted spinal tuberculosis. Three recovered without subsequent evidence of clinical tuberculosis.

### Association with Streptococcal Infection.

Spink (1937) reported that 41 patients (30·8%) of his 133 cases of erythema nodosum had tonsillitis or acute pharyngitis either before or during the eruption. Fifteen patients (11·2%) had rheumatic heart disease and in only 2 cases did erythema nodosum follow exposure to tuberculosis. Spink reasoned that streptococcal infections played a more important role in the aetiology of erythema nodosum than tuberculosis. However only 48 cases were subjected to x-ray examination of the chest. Eleven patients had recurrent erythema nodosum and one of these had otitis media which required drainage. In two other cases, erythema nodosum developed during convalescence from measles and in three others the cutaneous lesions were associated with dental abscesses. Spink particularly recorded that erythema nodosum appeared to be related to infection about the roots of teeth. One further case had gonococcal septicaemia.

Rollof (1949) found that of 42 cases of primary tuberculosis which originated with erythema nodosum, 21 had *Streptococcus haemolyticus* in the pharynx. In cases of primary tuberculosis, anti-streptolysin titres of over 200 A.U. were found to be considerably more frequent than in healthy children.

Doxiadis (1951) pointed out that the association of tuberculosis and erythema nodosum had already been accepted when the relationship of these skin lesions and haemolytic streptococcal infection was brought to the fore. " It was not therefore a matter of substituting one theory for another but of detecting the aetiological agent in those cases which could not possibly be due to tuberculosis. Thus, in most series there is an inverse relation between the incidence of tuberculosis and streptococcal infection."

### Association with Drugs.

In adults, Harold (1953) found that erythema nodosum was more often due to non-tuberculous causes including rheumatism, sarcoidosis and sulphonamide therapy. However Rollof (1950) believed that erythema nodosum occurring after sulphonamide therapy was related to tuberculosis. He recorded that the incidence of erythema nodosum in cases of primary tuberculosis was significantly higher when sulphathiazole was administered either therapeutically or experimentally.

In an earlier paper, Rollof (1945) reported a large series of cases of erythema nodosum occurring in connection with sulphathiazole treatment of fevers in children. He found that a tuberculous infection could frequently be incriminated. He considered that erythema nodosum was latent in the subcutis and was provoked by the catalyzation of sulphathiazole.

Vesey and Wilkinson (1959) observed that at one time sulphonamides were widely incriminated in the aetiology of erythema nodosum but it was difficult to know how often the eruption was due to the drug and how often to the infection for which it was given. They described a case of erythema nodosum following administration of sulphathiazole for cystic acne but they did not mention whether the chest had been examined radiologically.

### Other Causes and Special Features.

Two cases of erythema nodosum occurring in the third and fourth week of scarlet fever were described by Moritz (1934). Repeated serial tuberculin tests were negative ; there were no tuberculous contacts and skiagrams of the chest were clear. The one case tested still had a negative Mantoux reaction two months after discharge from hospital. These were the only patients who had persistently negative tuberculin reactions out of the 53 cases of erythema nodosum which Moritz saw in four years. In the course of measles, tuberculin hypersensitivity decreased and a positive von Pirquet reaction might become negative. In convalescence, the cutaneous reaction might become positive and Moritz reasoned that greater variations of allergic state might lead to the appearance of erythema nodosum.

Winer (1950) had a similar explanation for erythema nodosum occurring late in a tuberculous infection. It was probably the result of a loss of hypersensitivity after an acute infection such as measles and whooping cough. The return of hypersensitivity had the action of a new primary infection in promoting a reaction and therefore erythema nodosum might develop.

Postprimary erythema nodosum is a term which has been variously used to describe erythema nodosum developing in patients known to have been infected with tuberculosis a long time before the eruption. Wallgren commented that postprimary tuberculous erythema nodosum appeared during recovery from the new acute infection whereas the skin lesions in tuberculin negative children usually appeared during the progress of the acute infection and not after it had run its course. This dissimilarity indicated that the mechanism producing erythema nodosum was different in the two cases.

Doxiadis (1951) believed that infection causing a hypersensitivity to a bacterial allergen was an indispensable factor in the production of erythema nodosum.

Rice-Oxley and Truelove (1950) described four cases of erythema nodosum in females. All the lesions developed during an exacerbation of ulcerative colitis and were accompanied by fever. There were evidently a manifestation of the toxaemia and these observers suggested that the skin lesions might have been an allergic response to toxins present in the bowel comparable to the production of erythema nodosum in primary tuberculosis and streptococcal infection.

Bargen (1929) also described the association of erythema nodosum and

ulcerative colitis and Elitzak and Widerman (1941) related a similar combination. But in their three cases the Mantoux test was recorded as negative with high doses of tuberculin. The onset of the cutaneous manifestations was always at a time when the intestinal lesions became active.

Willcox (1952) enumerated measles, pertussis, lymphogranuloma venereum, gonorrhoea and coccidioidomycosis among the possible causes of erythema nodosum. Doxiadis (1951), however, in reviewing the rarer aetiological agents, rejected many of them as the skin lesions recorded with them did not conform to his description : viz. ulcerative colitis (Brooke, 1933), meningococcaemia (Collis, 1933), rat bite fever (Ripley and Van Sant, 1934) and gonorrhoeal septicaemia (Bakst *et al.*, 1935). He agreed that a strong case existed for accepting lymphogranuloma venereum (Hellerström, 1941) and trichophytosis (Bloch, 1921) among the infections in the course of which erythema nodosum might appear. It seemed that erythema nodosum was a non-specific syndrome always occurring during the active stage of various infections. Most of the reports on erythema nodosum following administration of iodides and bromides and similar drugs belonged to the early period of the study of this disease when no investigations were made for the presence of any infection.

Lutembacher (1955) wrote that erythema nodosum manifesting itself during the secondary stage of syphilis might be due to the re-awakening of latent tuberculosis.

Vesey and Wilkinson described a group of middle aged women with erythema nodosum and severe toxic symptoms following an exacerbation of chronic bronchitis.

Frankel (1945) similarly recorded erythema nodosum in middle-aged women with severe constitutional disturbances. Recurrent attacks and involvement of joints were common. There was no association with tuberculosis and the cause was thought most likely to be sensitization of the tissues by a streptococcal infection. A good prognosis was noted.

### Association with Bilateral Hilar Gland Enlargement and Sarcoidosis.

Crawley (1950), while remarking that the formerly widely held opinion of the rheumatic origin of erythema nodosum was fast disappearing, drew attention to its association with sarcoidosis. He cited three cases of erythema nodosum with bilateral hilar-gland enlargement and considered that the cause appeared to be sarcoidosis. But biopsy studies were not included and though serum protein estimations were performed, albumin globulin ratios were not quoted.

Vesey and Wilkinson also believed that bilateral hilar-gland enlargement and erythema nodosum represented an early stage of sarcoidosis and supported this statement by describing sarcoid tissues in biopsy specimens of skin or

glands in five cases. Besides the proved sarcoid cases, none of twenty cases of erythema nodosum and bilateral hilar gland enlargement had positive Mantoux reactions at strength 1 : 10,000. Iritis or conjunctivitis was present in four of these cases. A quarter of the twenty cases had radiographically abnormal hilar glands for over 18 months. In the remainder, the symptoms cleared and the chest signs reverted to normal in under 18 months. Seven of the twenty cases were markedly depressed and the symptoms were severe enough for three to be admitted to a mental hospital.

Six cases of erythema nodosum with bilateral hilar gland enlargement in relatively young women during the months of December to May were described by Dunner and Hermon (1952). Five cases had positive Mantoux reactions and one was negative at 1 : 10,000 strength. Tuberculosis as a cause was discounted, as bilateral hilar gland enlargement of this nature was not consistent with their present conception and experience of primary tuberculosis. There were no clinical manifestations of sarcoidosis and there were no bone changes in skiagrams of the hands and feet. Resolution of the hilar glands was usually complete within 6 months. So short a time, while not excluding sarcoidosis, was thought not to be in favour of it. They considered that these patients represented a special syndrome of uncertain aetiology.

Löfgren and Lundbäck (1952) by histopathological examination of specimens of skin, nasopharynx, bronchi and pulmonary parenchyma (obtained by bronchoscopy) and parotid gland showed that 26·4% of 212 cases of bilateral hilar-lymphoma syndrome had sarcoidosis. Subsequent tuberculosis was found in only one case. They used the term bilateral hilar-lymphoma syndrome to indicate the presence of large symmetrical hilar lymphomas with a negative or weak to moderate tuberculin reaction.

Kerley (1942) again described the association of erythema nodosum and sarcoidosis but his Case 12 could well demonstrate the provocation of erythema nodosum by sulphathiazole. He found that benign miliary infiltration of the lungs might occur simultaneously with the hilar gland enlargement or might not appear for some months. This was found in eight out of twelve cases. "A detailed study of the x-ray appearances in these 12 cases showed they were indentical with those found in the sarcoidosis of Boeck." In the same article, however, he wrote, "the relationship between erythema nodosum and Boeck's sarcoidosis although not absolutely proven is certainly probable."

In 24 cases out of 27 with erythema nodosum and bilateral hilar-gland enlargement, Geraint James *et al.* (1956) demonstrated sarcoidosis by a positive Kveim test (19 cases) and biopsies of skin, liver, lymph node, or directly from the erythema nodosum lesions (15 cases). The bilateral hilar lymphadenopathy always resolved, but in 5 patients it was followed by transient diffuse pulmonary mottling. In 17 patients, transient polyarthritis either preceded or accompanied the skin lesions. The syndrome had a favourable prognosis. They said

that it was important to obtain histological evidence to segregate this group from erythema nodosum due to other causes.

Wyn Williams and Edwards (1954) wrote "sarcoidosis is usually considered fairly rare; but, if cases are admitted on sound clinical evidence, we think it is relatively common". They went on to say that the recognition that this form of hilar adenopathy was usually caused by sarcoidosis would render the disease almost commonplace. However in the absence of any evidence indicating another disease, a benign sarcoidosis was the most likely explanation of most cases of bilateral enlarged hilar glands with or without erythema nodosum. They concluded by saying that it was possible that sarcoidosis was becoming more common.

Doxiadis (1951) was unable to find any reports of sarcoidosis and erythema nodosum in children.

In 9 cases out of the 100 who had erythema nodosum recorded by Johnson *et al.* (1951) at the Mayo Clinic, pulmonary hilar adenopathy was present. No disease process other than the skin lesions could be found to account for the hilar enlargement. In 4 of the 5 followed up the hilar-gland enlargement disappeared at the same time as the erythema nodosum. These authors summed up this vexing question succinctly. They wrote that if hilar adenopathy were found on roentgenologic examination of the thorax in a case of erythema nodosum the thought should be entertained, along with the consideration of other possibilities (notably tuberculosis, coccidioidomycosis and sarcoidosis) that the hilar enlargement might be simply a part of erythema nodosum of non-specific aetiology. Disappearance of the hilar enlargement might be anticipated as the erythema nodosum subsided. In none of the 15 cases considered to be due to sensitivity to drugs in this series of 100 cases was there hilar gland enlargement.

## Investigation.

With the general decline in tuberculosis, recent observers have tended to draw attention away from this disease as a cause of erythema nodosum. For this reason and because of the various views expressed above which may be thought to be diverse (though an explanation will be provided for this) a follow up study was conducted in this department of all cases of erythema nodosum which had occurred in the years 1948–58 inclusive.

It is the practice to admit all patients with erythema nodosum for investigation and rest in bed. Their case sheets were recovered by use of the World Health Organization's International Statistical Classification of Diseases. Doubtful cases were included in the follow up. Only some of the later cases were seen by the author when they had erythema nodosum.

The 115 cases to be described represent 0·91% of all admissions to this unit over the above period. Doxiadis (1951) found that the incidence of children with erythema nodosum admitted to a paediatric unit over a two-year period was 0·7 per hundred total admissions. However he did not admit all the cases of erythema nodosum that were seen.

The investigation was conducted as follows. All the patients were sent letters requesting them to attend hospital. They were interviewed and a note was made of

the illnesses they had suffered since discharge from this department. After a clinical examination, their chests and hands were radiographed. If there was then any indication for further investigations, they were carried out. Those that failed to attend were written to again asking them to reply to the following questions :— " What illnesses have you had since discharge from this hospital ? (Please give approximate dates and hospitals.) Have you or any of your family or close contacts had tuberculosis ? (Please give names, addresses, hospitals and approximate dates.) " Significant positive information obtained verbally or by letter from patients was checked by reference to the appropriate clinic. The names and addresses and dates of admission for erythema nodosum of those patients that still failed to respond were then given to the Public Health Departments of Liverpool and adjacent areas to see if any patients or any of their families had been notified as tuberculous.

This investigation was carried out during the mass x-ray campaign in Liverpool (1959) and many of the patients written to replied that their chest films taken during this survey were clear.

## Results.

*Age incidence.*—Patients in all age groups were admitted to hospital. It will be seen from Table I that the female age incidence was maximal during the 15–24 years period and this peak was similar to that for notifications of new cases of tuberculosis in Liverpool females (see Table II ; for convenience, only 6 years are tabulated but in each of the years 1948–58 inclusive the highest incidence of tuberculosis in Liverpool females was in the 15–24 years group).

Table I.—*Age and Sex Incidence of Cases of Erythema Nodosum.*

| Age period (years) | 0–5 | 5–15 | 15–25 | 25–35 | 35–45 | 45–55 | 55–65 | 65 and over |
|---|---|---|---|---|---|---|---|---|
| Male cases | — | 6 | 1 | 4 | 1 | 1 | — | — |
| Female cases | 2 | 15 | 44 | 11 | 18 | 8 | 2 | 2 |
| Total | 2 | 21 | 45 | 15 | 19 | 9 | 2 | 2 |

Table II.—*Primary Notifications of New Cases of Respiratory Tuberculosis in Liverpool Females from the Annual Reports of the Health of the City of Liverpool).*

| Age period (years) | 0–5 | 5–15 | 15–25 | 25–35 | 35–45 | 45–55 | 55–65 | 65–75 | 75 and over |
|---|---|---|---|---|---|---|---|---|---|
| 1950 | 48 | 57 | 287 | 195 | 79 | 44 | 26 | 15 | 5 |
| 1951 | 48 | 55 | 265 | 188 | 89 | 47 | 20 | 10 | 1 |
| 1952 | 48 | 83 | 293 | 155 | 95 | 49 | 40 | 9 | 5 |
| Notifications of tuberculosis (new cases, all types) in Liverpool females. | | | | | | | | | |
| 1956 | 26 | 45 | 189 | 119 | 74 | 30 | 13 | 7 | 10 |
| 1957 | 31 | 53 | 151 | 103 | 81 | 43 | 27 | 16 | 4 |
| 1958 | 33 | 40 | 106 | 69 | 41 | 26 | 20 | 10 | 8 |

The percentage of positive tuberculin reactors of large numbers of Liverpool school children, aged 13 or 14 years (shown by tuberculin jelly tests, doubtful and negative reactors were Mantoux tested).

| | |
|---|---|
| 1954 | 34·0% |
| 1955 | 27·9% |
| 1956 | 28·1% |
| 1957 | 21·5% |
| 1958 | 19·2% |

Spink found that the highest incidence of erythema nodosum was in the 20–29 years age group. Johnson *et al.* described an age incidence rising and falling away from a peak in the 30–50 years of age range. Doxiadis wrote that erythema nodosum could only be called a disease of childhood in males for in females the highest incidence was observed in the 15–25 years age group. Vesey and Wilkinson recorded that the age distribution in their series rose to a peak in the 40–50 years age group and then fell. They wrote that this distribution was that of a community in which adult primary tuberculosis is uncommon.

I suggest that in contrast to the last series, the maximum age incidence described first occurred at an earlier period in life because of the relative frequency of primary tuberculosis in the young adult female population of Liverpool.

*Sex incidence.*—Table I shows that both in childhood and adult life, erythema nodosum appears to be predominantly a female disease, but this is more marked in the older age group. Altogether, 102 cases (88·7%) were in females and 13 (11·3%) in males.

Doxiadis (1951) wrote that even in childhood there was a higher incidence of erythema nodosum in the female sex. Spink noted 111 females and 22 males in a series of 133 cases of erythema nodosum. Before puberty it was noted that the sex incidence was about evenly distributed but after that there was a sharp increase in the number of females. Perry found that in 112 cases of erythema nodosum of all ages, the sex incidence was roughly 2 : 1 with a preponderance of females. Under 15 years of age there were 36 boys and 31 girls whereas over this age there were 43 females and only 2 males. In 70 adult cases of erythema nodosum, Vesey and Wilkinson found that 54 were female and 16 male. Johnson *et al.* recorded 77 female cases and 23 male in 100 cases of erythema nodosum of all ages. Concerning erythema nodosum in children, Booth wrote that before the age of puberty the sex incidence was about equal but after puberty, female sex hormones may be a contributory factor in producing the higher incidence of the disease in women.

It would however be equally pertinent to say that the lower incidence in men is due to the fact that the legs and arms are well protected from the cold by clothing (in contrast to women) as to say that hormonal influences are involved. No explanation is offered for this phenomenon of differing sex incidence.

*Seasonal incidence.*—Table III shows a slight increase in erythema nodosum in the colder months of the year.

Michelson (1958) wrote that the late fall, winter and early spring were the times of commonest occurrence of erythema nodosum. Booth agreed and said the incidence reached a low level in summer and early fall. Spink recorded that the greatest number of cases occurred in early spring, with a low level in midsummer gradually rising early in the fall. This curve closely followed the sea-

TABLE III.—*Seasonal Incidence of Cases of Erythema Nodosum.*

| Year | Jan. & Feb. | Mar. & Apr. | May & June | July & Aug. | Sept. & Oct. | Nov. & Dec. |
|---|---|---|---|---|---|---|
| 1948 | 2 | — | — | — | — | 1 |
| 1949 | — | 2 | 1 | 1 | — | 2 |
| 1950 | 4 | 3 | 1 | — | 2 | 1 |
| 1951 | — | 4 | 2 | 2 | — | 2 |
| 1952 | 2 | 2 | 1 | — | 1 | — |
| 1953 | 7 | — | 2 | 1 | — | 3 |
| 1954 | 1 | 4 | 2 | 2 | 2 | 2 |
| 1955 | 1 | 2 | 4 | 4 | 1 | 5 |
| 1956 | 3 | 3 | 3 | — | 1 | 1 |
| 1957 | 1 | 3 | — | 2 | 6 | — |
| 1958 | 2 | 2 | 2 | 4 | 1 | 2 |
| | 23 | 25 | 18 | 16 | 14 | 19 |

sonal incidence of 95 cases of acute tonsillitis (other streptococcal infections such as scarlet fever and erysipelas have the same seasonal incidence as tonsillitis). Spink did not offer this relationship as a proof that erythema nodosum was a manifestation of streptococcal infection but suggested that it must be considered along with the other data presented in his study. Doxiadis (1949) also confirmed that the lowest incidence of erythema nodosum cases occurred in summer and autumn.

As streptococcal and respiratory infections are incriminated in the aetiology of erythema nodosum, it is not surprising to find the highest incidence during the colder months.

## ANALYSIS OF CASES AND FOLLOW UP.

Only one investigation was common to all the patients while they were in hospital—radiograph of the chest—and this was perhaps the most rewarding of all the examinations which have been made on erythema nodosum patients.

The aetiological agents are classified in the following groups :

(i) Tuberculosis.
(ii) Tonsillitis and sore throat.
(iii) Hilar gland enlargement, bilateral or predominently unilateral but without subsequent tuberculosis.
(iv) Miscellaneous.
(v) Unknown.

While the aetiology of group (ii) was probably mainly streptococcal infection (bacteriological confirmation of this was lacking in some cases) it must be admitted as Doxiadis (1951) has pointed out, that other agents apart from the haemolytic streptococcus may be the cause of an acute tonsillitis.

(i) Nineteen cases had tuberculosis at the time of the skin lesions or shortly after, including a patient who had a tuberculide and who later, unknown to me, developed pulmonary tuberculosis. Three other patients subsequently developed pulmonary tuberculosis diagnosed at other clinics. Three patients had tuber-

culous contacts about the time of the skin manifestations but only one of this group developed tuberculosis. The other two are classed as suspected tuberculosis but not proven (see Familial Disease and Erythema Nodosum). In all, 24 patients are included in this tuberculous group (20·9%). Unfortunately many of the results of Mantoux reactions were not available. All the cases of tuberculosis found when the skin lesions were present were of the primary type. Pautrier (1955) considered that when tuberculosis is concomitant with erythema nodosum it is of the primary type except when massive re-infection produces a bacillaemia.

Only three male patients were placed in group (i) and two of these were classed as suspected tuberculosis. Of the twenty-one female patients with frank tuberculosis, thirteen were between the ages of 10 and 20 when this disease was diagnosed.

From the Liverpool Public Health Department's case rates of tuberculosis for 1948–1958 inclusive, the average incidence of respiratory tuberculosis each year for this period was 1·66 cases per 1,000 population. Similarly the average incidence of non-respiratory tuberculosis was 0·18 cases per 1,000 population.

(ii) Eight cases had tonsillitis or sore throat and one had mitral stenosis but had had rheumatic fever in childhood. There were no joint pains or joint swellings in this case which is hesitantly grouped here. In all, 9 cases (7·8%) are included in this group.

(iii) Fifteen patients (13%) had hilar gland enlargement and one of these was known to have sarcoidosis.

Excluding the latter, 9 of these patients returned and had radiographs of the chest and hands. Nothing abnormal was found in any of these but two chest films still showed hilar gland enlargement. In one case, the glands were smaller than when the patient was first seen. Further haematological investigation was refused. In another, the glands showed no change in size but blood counts, serum protein and A.G. ratio estimations were normal. This patient's Mantoux reaction was negative at strength 1 : 1000 when she had erythema nodosum. The case considered to have sarcoidosis was diagnosed by virtue of the bilateral hilar gland enlargement on the chest film, negative Mantoux reactions to serial tuberculin tests, reversal of A.G. ratio and cystic change in a metacarpal shown in a radiograph of the hand. Altogether 40 patients returned, 39 had radiographic examination of the hands, and 38 were normal. Clinically all were well.

(iv) One patient on admission had pains in the lower abdomen and was transferred to a gynaecological unit for the treatment of incomplete abortion. Another was five months pregnant on admission and the erythema nodosum recurred with the next pregnancy. A further woman was three months pregnant on admission. Fry described erythema nodosum in a four months' pregnant woman. Löfgren and Lundbäck (1952) found that in 107 female cases of erythema nodosum (in their series of 212 bilateral hilar lympho-

mas) 24 developed nodal fever during the period of lactation. Three cases developed erythema nodosum during pregnancy and in another 5 it appeared within one year of delivery but after weaning. They supposed that the relation demonstrated might be due to a decrease in resistance to the aetiological agent of the disease during pregnancy or lactation.

An unusual occurrence was that of a girl of 16 who had erythema nodosum and four years later was operated on for Crohn's disease. Cecil and Loeb (1959) say that there is a strong histological resemblance between Crohn's disease and tuberculosis and sarcoidosis, though a definite relationship has not been demonstrated. It is possible that regional ileitis is a non-specific pathological response to a variety of inciting agents.

Two women had hypochromic anaemias of between 50 and 60%. Neither was satisfactorily diagnosed but the one that returned to the follow up (4 years later) reported that she had recently been treated for a duodenal ulcer.

Three patients were suffering from exacerbations of chronic bronchitis at the time of the erythema nodosum and a fourth was shown by radiographic examination to have a partial atelectasis of the middle lobe of the right lung.

One young woman exhibited the lesions of herpes febrilis while another was treated for gingivitis and carious teeth.

A woman of 57 complained that she had had arthritis of the fingers for some years. This was of a mild rheumatoid type. (No rheumatoid changes were evident clinically in other joints.)

(v) In 54 patients (47%) the erythema nodosum was unexplained and was not associated with other diseases or syndromes.

Three cases had a further attack of erythema nodosum and in agreement with the present view, active tuberculosis was not demonstrated in these patients (Vesey and Wilkinson). A history of a previous attack was given by 13 patients in Perry's series. All were female and all were tuberculin negative but the 4 cases tested were sensitive to streptococcal nucleoprotein.

A woman of 26 with erythema nodosum had had tuberculous disease of the hip when she was a child of 12. Another young woman had had pulmonary tuberculosis but developed erythema nodosum three years later. Both parents of this last patient had died of tuberculosis. It would seem that the last two cases should be classed as erythema nodosum of unknown origin as the tuberculous disease which they had previously exhibited was inactive at the time of the skin lesions.

### Familial Disease and Erythema Nodosum.

One patient was suspected to have had a tuberculous infection because shortly after he acquired erythema nodosum his brother was notified as suffering from pulmonary tuberculosis (information supplied by the Liverpool Public Health Department at the time of the follow up).

The sister of another patient had erythema nodosum and primary tuberculosis (treated at another hospital) five weeks after my patient exhibited the skin lesions, but tuberculosis was never proven in my case in fact at the time of writing he was serving in the army.

The sister-in-law of a further patient had recently entered a sanatorium for treatment of pumonary tuberculosis prior to my patient's manifesting erythema nodosum. Primary tuberculosis was demonstrated in my patient by radiographic examination of the chest.

It is possible but not proven that both the first two patients were infected with the tubercle bacillus and erythema nodosum resulted. However the infection was overcome by the patient without producing recognizable signs of tuberculosis. The recording of a changing Mantoux reaction from negative to positive at the time of the skin lesions would have lent support to this hypothesis (see below).

Harold (1953) describes a family in which the three children had erythema nodosum in an eight-week period. All the children had their chests examined radiologically. They were clear and the Mantoux reaction was positive in all. The mother was found to have open tuberculosis and the family had all slept in one room a month prior to these episodes. Harold remarks that these cases are unusual, " in that recognition of erythema nodosum in the children led to the detection and early treatment of a symptomless parental source of tuberculosis."

Roosvall (1936) put forward the view that erythema nodosum might take place as the manifestation of tuberculous infection because the patient had a special disposition to the disease. In support of this view he said that in certain families erythema nodosum was very common after a tuberculous infection while in other families none of the infected exhibited erythema nodosum. Whether erythema nodosum occurred or not depended to a great extent " on the familial constitutional mode of reaction of the tuberculous infected individual." Michelson described a boys' school of 173 pupils ranging in age from 10 to 19. Epidemic erythema nodosum occurred in 14 pupils. He wrote that in 12 of these patients hilar glands or the childhood type of tuberculosis were found. One hundred and thirty-nine out of 158 boys tuberculin tested reacted positively. A boy with open tuberculosis had been removed from the school five weeks before the epidemic. Booth found two families in her series with two or more cases of erythema nodosum. In the first the tubercle bacillus was incriminated while in the second the streptococcus was thought to be the causal agent.

Erythema nodosum does not develop in all cases of tuberculosis, haemolytic streptococcal infection, coccidioidomycosis etc., and therefore Booth considered, it was necessary to postulate that there must be a heriditary predisposition of certain individuals to respond to various infections in this manner. Fry

recorded a family in which the father was diagnosed as an open tuberculous case. The children were described as tuberculin negative. Within three months the mother (who was pregnant) and two of the three children developed erythema nodosum. All then had positive tuberculin tests. Up to fifteen months later, follow up radiographs of the erythema nodosum cases were normal. Perry elicited a family history of erythema nodosum in ten cases in his series. One family had three children with erythema nodosum which led to the discovery of a tuberculous father.

### Delayed Tuberculosis.

One patient, a girl of 18, was thought to have had a tuberculous skin lesion at the time of the erythema nodosum. Three years later, pulmonary tuberculosis was found in another clinic. The chest film of another girl, aged 16, was normal when she was admitted. However, later in the same year pulmonary tuberculosis was diagnosed elsewhere. (The latter finding was reported to us *via* the records of the Liverpool Public Health Department.) The chest film of a third girl, aged 19, was also clear when she was admitted for erythema nodosum. Two years later pulmonary tuberculosis was found in another clinic. A further girl of 16 developed pulmonary tuberculosis six years after an attack of erythema nodosum when a normal chest film was demonstrated. Owing to the lapse of six years between these two observations it is hardly likely that the erythema nodosum and tuberculosis were connected in this instance. Pulmonary tuberculosis was demonstrated at this clinic in yet another girl of 16, seven months after the onset of erythema nodosum. A child of 9 had a strongly positive Mantoux reaction but the chest film was normal shortly after she was admitted to hospital. Within two months, a primary tuberculous complex appeared on a chest radiograph. In four other cases, pulmonary tuberculosis was shown at this clinic to have occurred within several months of finding a clear chest radiograph at the time of the skin lesions.

Cray (1945) thought that every case of erythema nodosum should be regarded as a newly infected case of tuberculosis. "Therefore search should be made among family and friends for the unknown source of infection." Paul and Pohle (1941) considered that all patients with erythema nodosum should be subjected to radiographic examination of the chest as part of the routine procedures on such cases. "Even when this is negative follow up examinations should be done before the patient is considered to be free from tuberculosis." Dunner and Hermon substantiated these remarks and over twenty-five years ago Collis (1933) wrote, "It is not too much to say dogmatically that our attitude to erythema nodosum should be to regard every case as tuberculous till proved otherwise."

### Prognosis of Tuberculous Erythema Nodosum.

Wallgren gave evidence to show that in tuberculous erythema nodosum the infection took place three to eight weeks prior to the appearance of the skin lesion. He considered that erythema nodosum should be regarded as a favourable syndrome and that the prognosis was certainly not worse than in primary tuberculosis without erythema nodosum. For it ensured that the diagnosis was made at a very early stage thus making it possible to commence appropriate treatment early in the infection.

Doxiadis (1951) summarized the controversy as to the prognosis in primary tuberculosis with or without erythema nodosum by saying that the course and prognosis of a primary tuberculous infection with erythema nodosum was more severe when compared with other cases of primary infection most of which were detected because of the conversion of the tuberculin reaction, but that the course and prognosis were not different if the comparison was made with cases of primary tuberculous infection with clinical and radiological manifestations in addition to the positive tuberculin reaction.

### Racial Differences.

Paul and Pohle recognized that the chief causes of erythema nodosum might vary in different countries or in different parts of the same country. Wallgren recorded that in Sweden only 5% of the cases of erythema nodosum are non-tuberculous whereas in England the percentage is six times greater. Roosvall wrote that erythema nodosum tuberculosorum occurred most commonly in Scandinavia and England. In the Latin countries, the disease was rather rare and it occurred relatively seldom in Hungary. Variation in frequency was considered by this author to be due to racial differences.

It is clear that climate, standards of living and perhaps familial and racial characteristics would influence the degree in which the different aetiological agents were incriminated in any survey of erythema nodosum cases. These results would be further modified by the thoroughness and interpretation of investigations carried out on these patients.

### Investigations.

A case has already been made for radiography of the chest. Besides routine blood counts and urine examinations, serial and repeated tuberculin tests, serum protein with A.G. ratio estimations and biopsy of various tissues help to differentiate the sarcoid and tuberculous patients. Culture of a throat swab and the more refined examination of streptolysin titres throw light on a streptococcal infection. Erythrocyte sedimentation rates help in following the course of the disease. Naturally the trend of investigations depends on the clinical findings but these are often inconclusive. However, if the most serious diagnoses

are eliminated it cannot be to the detriment of the patient if the exact aetiology is not determined.

## Treatment.

The treatment should be directed towards the cause where known. In the initial stages of the disease the patient should mostly be confined to bed.

It has been the practice in this clinic to withhold treatment from erythema nosodum cases of unknown origin as their progress with rest in bed alone has been satisfactory. Salicylates however are of help by reason of their antipyretic effect and where joint pains are a feature, the analgesic properties of these compounds are welcomed.

Lutembacher stated that cortisone in contrast to salicylates did not affect the general evolution of erythema nodosum ; if steroid therapy were stopped prematurely the disease would recommence and proceed unaltered in character. Albeaux-Fernet *et al.* (1954) gave cortisone with a " cover of streptomycin " to a severe case of erythema nodosum for six weeks. They found that if therapy was stopped sooner than this there might be a recrudescence of the disease. In the very severe case where cortisone may be given it is clear the the clinician must pay careful heed to the possibility of tuberculous disease being present.

If a strongly positive Mantoux reaction accompanies the erythema nodosum and tuberculous infection is suspected, then anti-tuberculous therapy is indicated even in the absence of radiological signs. If this therapy is not administered it is likely that in some of these cases the tuberculous infection will progress.

As the skin lesions are self limiting local treatment is usually unnecessary.

## Conclusions.

Erythema nodosum was merely a passing phase in an otherwise healthy life in the majority of these cases. Chest complications however are sufficiently common for a radiograph of the chest to be mandatory in all these patients.

Infection with the tubercle bacillus may produce erythema nodosum (and infection will result in sensitivity to tuberculin) but tuberculous disease is not necessarily a consequence.

If tuberculous disease is to be eradicated from the community, it is suggested that patients with erythema nodosum should be followed up for a period of not less than two years in case tuberculosis supervenes (e.g. chest radiograph every six months). Even when the skin disease is thought to be a manifestation of another cause, a similar surveillance is suggested as tuberculosis may yet reveal itself. It is recommended that close contacts of patients with erythema nodosum should be investigated where there is the slightest suspicion of tuberculosis. Although this kind of enquiry will frequently be negative, those occasions when further disease is located should make it worth while.

It is possible that in areas where tuberculosis is still relatively common, notification of all cases of erythema nodosum to the Public Health authority would promote the fight against tuberculous disease. Further enquiry could then be pursued through the medium of a Contact Tuberculosis Clinic.

## Summary.

A follow up study was conducted on 115 cases of erythema nodosum. Information was received about 66 patients (57·4%).

Twenty-two patients contracted pulmonary tuberculosis and two others were suspected of having been infected with the tubercle bacillus (in all, 24 cases i.e. 20·9%).

Nine cases (7·8%) were probably streptococcal in origin.

Fifteen patients (13%) showed bilateral hilar-gland enlargement.

Thirteen patients (11·3%) suffered from various other maladies and in 54 cases (47%) no disease, apart from the skin lesions, was found.

It is recommended that cases of erythema nodosum should be followed up with radiographs of the chest every six months for a period of two years. Their close contacts should often be investigated for latent tuberculosis.

I wish to thank Dr. F. Glyn-Hughes and Dr. C. McGibbon for their helpful criticism and advice. I am grateful to Dr. E. Walker for his radiological interpretations and to Professor A. B. Semple for providing information from the records of the Liverpool Public Health Department. My thanks are due to Miss C. Ledsham and records staff for recovering case sheets and for clerical work.

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# ATOPIC ECZEMA IN EUROPEAN AND NEGRO WEST INDIAN INFANTS IN LONDON.

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The influx of negro West Indians into Britain during the past few years has been responsible for our particular interest in certain skin diseases among these people. The Belgrave Hospital for Children would appear to be ideally situated for making comparative studies of West Indian and European children since it draws its patients from the Brixton area which has approximately 5000 West Indian inhabitants. During the past year we have made a study of infantile eczema in 44 West Indian and 50 European infants under the age of two years.

## Incidence.

The high incidence of eczema among infants of West Indian parents was striking. We found that approximately 40% of all infants up to the age of two years suffering from infantile eczema were West Indian. On the other hand, out of 100 consecutive patients attending the Casualty Department of the Belgrave Hospital only 9 were West Indian. Similarly out of 1378 new patients referred for haematological investigation at the same hospital 140 (10·2%) were West Indian. These figures suggest that in this country the incidence of infantile eczema in the age group 0–2 years is relatively higher in the West Indian population than in European children of the same age.

Infantile eczema, however, appears t< be uncommon in tropical countries. Clarke (1959) stated that eczema of endogenous origin was distinctly rare in the African. Dr. D. B. Jelliffe (1959) found that among Jamaicans of predominantly African descent, eczema was rare in the lower income groups. Drs. E. H. Back and F. W. Jacobson of the University College Hospital of the West Indies have kindly supplied us with information concerning the incidence of this condition at their hospital. Between 1952 and 1959 the Pediatric and Dermatological Departments recorded only 39 cases of infantile eczema under the age of 2 years.

Although it is difficult to obtain an accurate assessment of the relative incidence of infantile eczema among West Indians living in London and those living in the West Indies, there seems little doubt that the incidence is much higher in London. This, or course, may be real or only apparent. Such an apparent increase might be due to incomplete statistical data concerning the incidence of the condition in the West Indies, a greater "disease awareness" in this country may bring more cases to hospital and easy availability of hospital services in the country may be responsible for patients being seen with milder forms of the disease.

## Family History.

It is interesting to note that of the 50 European children with infantile eczema, a family history of atopy (atopic eczema, asthma, hay fever) was obtained in 32 (64%) but among the 44 West Indian children only 3 (7·5%) gave such a history. In two of these a sibling had atopic eczema while the mother of the third suffered from asthma. Thus a family history of atopy is common in the European but rare in the West Indian. Such a striking difference is not easy to explain. While factors such as an unreliable history or incomplete information about relatives in the West Indies might contribute to this difference, they would not account for the marked discrepancy between the two races.

In contrast to these findings, the incidence of allergic manifestations among the eczematous infants themselves was not significantly different, several developing asthma in addition to their eczema.

## Clinical Features.

Only cases conforming to the classical clinical picture of infantile eczema were included in this study. Cases of so-called seborrhoeic eczema in which the eruption was wholly or mainly confined to the seborrhoeic areas were excluded. However, it must be admitted that the dividing line between these two conditions was often difficult to define and certain cases originally diagnosed as seborrhoeic eczema subsequently developed the features of atopic eczema.

In our series, the times of onset of the eczema in the West Indian and European infants were similar and the severity of the disease process was not significantly different in the two groups. However, certain points of difference were noted. As might be expected, pigmentary changes associated with infantile eczema were much more striking in the West Indian infant. Patches of hyperpigmentation or hypopigmentation were often seen at the sites of previous eczema, but in a number of cases macular hypopigmented patches, particularly on the cheeks, were a presenting feature. As the scaling over such patches was only just perceptible, these cases were often incorrectly diagnosed by the general

practitioner as vitiligo or even leprosy. With appropriate treatment of the overlying eczema, these areas gradually regained their pigment.

In other cases, aggregations of small closely set rounded papules were seen on the back, chest and abdomen. At times these lesions resembled the rare lichen scrofulosorum, but typical eczematous patches were usually present in other areas. Although the incidence of ichthyosis vulgaris was the same in the two races, we gained the impression that eczema associated with widespread desquamation occurred more often in the West Indian infant. Similarly lichenification, especially of the flexures, was sometimes present to a striking extent in the West Indian, but this was by no means an invariable finding. We have not found any obvious difference between the European and West Indian infant in their response to treatment, but whether their ultimate prognosis will be the same can only be decided after a prolonged period of observation.

It is perhaps interesting to note that the West Indian infant suffering from infantile eczema possesses no immunity to infection with vaccinia virus, since in our series the only case of Kaposi's varicelliform eruption followed vaccination of one of these infants.

Twenty-five of the West Indian infants (62·5%) had one or more Mongolian spots. The slate blue patches varied in diameter from one quarter of an inch to several inches. The commonest site was the sacral area, but lesions also occurred on the lumbar region, buttocks, legs and arms ; occasionally even the hands and face were involved.

## Laboratory Findings.

(i) *Incidence of anaemia.*—In another paper (Davis *et al.* 1960) we have shown that in the age group 0–2 years, iron deficiency anaemia occurred twice as often in the West Indian as in the European infant. The various aetiological factors were discussed, but it was pointed out that the presence of eczema was of no importance in this respect. Conversely, the haemoglobin level does not appear to have any direct bearing on the severity of the eczema nor was there any convincing evidence that a rise in haemoglobin was followed by improvement in the eczema.

(ii) *Total and differential white cell counts.*—These were made on 41 European and 32 West Indian infants with eczema at their first attendance. White cell counts were also carried out on a control group of 39 healthy European and 27 West Indian infants attending local day nurseries. The only differences between these four groups were in the absolute numbers of eosinophils. In the control groups, all the West Indian and all except two of the European infants had normal absolute numbers of eosinophils (Wolman, 1957). In contrast, an eosinophilia was found in 16 out of 32 of the West Indian infants with eczema

(50%) and in 14 out of 41 (34%) of the corresponding European infants. Not only was the incidence of eosinophilia higher in the West Indian infants, but higher absolute numbers of eosinophils were also found. Thus, the highest initial count recorded in a West Indian infant was 8260 eosinophils per cu. mm. compared with 2760 per cu. mm. in a European infant. The reason for the higher eosinophilia in the West Indians is not clear, but various possibilities were considered. A higher incidence of asthma or more widespread eczema in the West Indian group was not responsible for the increased eosinophilia. Likewise the absence of ova in the stools eliminated worms as a possible factor. As all the infants were born in this country and had never visited the West Indies, tropical eosinophilia could be dismissed. It seems possible that the increased eosinophilia observed in the West Indians may indicate a difference in racial response. In a number of the West Indian and European infants eosinophil counts were repeated on four or more occasions. Several children showed an individual tendency to maintain a certain eosinophil level, high or low, in successive counts. The degree of eosinophilia did not appear to have any prognostic significance and bore little relation to the severity of the eczema.

(iii) *Abnormal haemoglobins.*—The sickle cell trait was detected in only two (4·6%) of our West Indian infants, a figure which is slightly lower than the average (6·7%) of all West Indians attending this hospital. Routine electrophoresis of the haemoglobins was not carried out but it was performed whenever the blood film suggested the possibility of a haemoglobinopathy. In this series, one infant had numerous target cells on the stained film and the electrophoretic pattern showed haemoglobins A and C.

(iv) *Stools.*—Stools and cellophane swabs from 28 West Indian infants were examined but, as already mentioned, no ova were found.

## Summary.

A comparative study of atopic eczema in European and West Indian infants is reported.

The high incidence of this condition among West Indian infants in London is contrasted with its apparent rarity in the West Indies. Possible reasons for this are given.

Sixty-four per cent of the European but only 7·5% of the West Indian infants had a family history of atopy. Certain clinical differences between eczema in the West Indian and European infant are briefly mentioned.

Iron deficiency anaemia was found more frequently in the West Indian and responded satisfactorily to oral iron. No correlation existed between the degree of anaemia and the severity of the eczema and correction of the anaemia was not followed by improvement in the eczema.

Among the eczematous infants, eosinophilia was more marked and occurred more frequently in the West Indian. Tropical eosinophilia and intestinal worms

were not responsible and the incidence of asthma or the severity of the eczema was no greater in the West Indian. Thus the reason for the greater eosinophil response in those West Indian infants is not clear, but may represent some inherent racial difference.

Among a control group of healthy infants, the incidence of eosinophilia was no greater in the West Indian than in the European.

We thank Mr. William C. P. Pakeman, Medical Records Officer, University College Hospital of the West Indies, for his help with the statistical data.

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# ULCERATION OF THE SKIN IN MULTIPLE MYELOMA.

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Bluefarb (1955) classified the skin changes associated with multiple myeloma. He divided them into specific lesions caused by plasma-cell infiltration, " toxic " eruptions and those due to abnormal proteins, blood cytopenias and myelomatous involvement of internal organs. Ulceration of the skin occurring in the presence of cryoglobulinaemia has been reported on several occasions (Flemberg and Lehman, 1944 ; Flemberg, 1948 and Rörvik, 1950). It is of two types : one occurs on areas exposed to cold and is associated with Raynaud's phenomenon, the other on areas overlying abundant subcutaneous fat which is infiltrated with plasma cells. Rörvik postulated that this second type of ulceration which occurs in regions not unduly exposed to cold was due to a combination of the relatively poor circulation in adipose tissue and the blood changes of myeloma.

The case reported below is of interest because indolent ulceration, similar to that reported by Hicks (1950) under the heading of " Ulcus Migrans ", occurred as a complication of unsuspected myeloma with hypogammaglobulinaemia, in the absence of circulating cryoglobulins.

## Case Report.

A retired railwayman aged 74 was well until 1955, when he began to develop skin lesions on the upper chest and back. They started as painless papules which enlarged, ulcerated, crusted and healed spontaneously in two to three weeks, leaving purple scars one to two centimetres in diameter. These areas gradually became pale, depressed and atrophic. The lesions have recurred at frequent intervals. In December 1959, he was first seen at another hospital with a similar lesion on the left flank. At this time blood count was normal, E.S.R. (Westergren) was 25 mm. in the first hour and slight proteinuria was present. During the next ten months, treatment included local antiseptic applications, oral tetracycline and sedation. However, the ulcer on the flank gradually enlarged and new lesions continued to appear. He was admitted to hospital in October, 1960 and a further ulcer developed on his left arm. The ulcers were treated with hydrocortisone and teramycin ointment and he was given courses of furaltadone (Altafur), sodium methicillin (Celbenin) and prednisolone without effect. At the end of November 1960, he was transferred to the Slade Hospital, Oxford, for further investigation. He felt perfectly well throughout.

Examination showed an obese, healthy-looking man with old acne scars on the chest and back where there were also many scarred atrophic areas one to two centimetres in diameter. Over the lateral aspect of the left iliac crest (Fig. 1) there was an ulcer 20 cm. long, 4 cm. wide and 0·5 to 1·5 cm. deep. Its outline was serpiginous, the floor consisted of granulation tissue, the edge was raised, oedematous and purple, pus exuding from undermined areas, and the base and surrounding tissues were indurated. A similar, though smaller ulcer was present over the lateral aspect of the left deltoid

muscle. There was no local lymphadenopathy. Further clinical examination was normal except for multiple premature systoles and a left indirect inguinal hernia ; the blood pressure was 140/80.

*Investigations.*—Hb. 14·2 g.%, W.B.C. 6800 per cu.mm. (normal differential), E.S.R. (Westergren) persistently between 70 and 100 mm. in the first hour. No L.E. cells were found. The urine contained Bence-Jones protein and between 3 and 6 grams of protein were lost daily (Esbach). Blood urea 35 mg.%. Repeated aerobic and anaerobic culture from ulcer swabs negative. Wassermann and Kahn reactions negative.

Serum proteins on two occasions : total 8·5 g. %, albumin 3·5 g. %, globulin 5·0 g. % ; and total 7·9 g. %, albumin 3·3 g. %, globulin 4·6 g. %.

Electrophoresis : albumin 37%, $\alpha_1$-globulin 16%, $\alpha_2$-globulin 34%, pre-$\beta$-globulin 4%, $\beta$-globulin 6%, $\gamma$-globulin 3%. There was an intense myeloma-like band in the

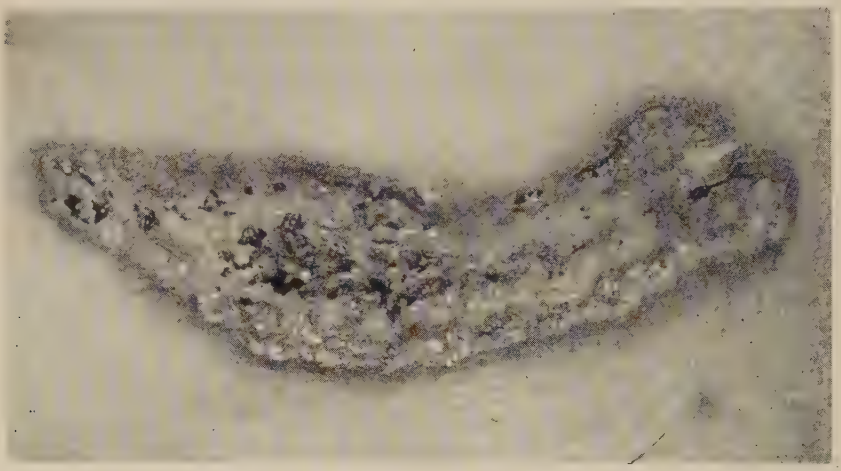

Fig. 1

$\alpha_2$-globulin region, an abnormal globulin band in the pre-$\beta$ region, and a gross reduction in $\gamma$-globulin. There were no circulating cryoglobulins. The reduction of $\gamma$-globulin was confirmed by a $\gamma$-globulin neutralization test which showed that the patient's serum had about one fifth the ability of a control serum to neutralize anti-human globulin serum, using as the indicator red cells coated with immune antibody. Serum complement was also reduced.

Chest x-ray showed some enlargement of the heart to the left and increased basal lung markings. Skull, lumbar spine and pelvic x-rays showed no evidence of myeloma or osteoporosis. Sternal marrow (Dr. F. Bolton) : " a cellular sample of marrow was readily obtained. It contained large numbers of plasma cells varying from 30 to 50% of the marrow cells in different parts of the slide. The majority of cells had normal plasma cell morphology ; however, quite a number of multinucleate forms with up to seven nuclei were present and there were occasional cells with large nucleoli. In association with the hypogammaglobulinaemia the findings suggested that these were myeloma cells rather than plasma cells arising as a result of chronic infection."

Histological report on a biopsy taken from the edge of the ulcer of the left flank (Dr. W. A. Aherne) : " at one end the epidermis was rather deeply invaginated into the dermis and part of the wall of the sinus thus formed appeared necrotic. There was a heavy infiltrate of lymphocytes and plasma cells and to a lesser extent poly-

morphonuclear leucocytes in relation to the necrotic material. Further out there was a rather marked histiocytic proliferation which was presumably secondary to the escape of keratinized material. The plasma cells appeared to be normal. Deep to the inflammatory process there was a zone of scarring. The appearances were those of a non-specific inflammatory ulceration."

*Progress.*—Following the patient's transfer to Oxford, prednisolone was continued in daily doses of 20 mg. Wet dressings of eusol were applied to clean the ulcers which were then treated by insufflation with neomycin and bacitracin powder. The edges of the ulcers became less oedematous and lost their purple colour, the granulation tissue became cleaner and epithelialization commenced. A course of $\gamma$-globulin which had been contemplated at one time in view of the hypogammaglobulinaemia, was considered unnecessary as the ulcers began to heal. By the end of December, 1960 the ulcer of the flank had reduced in size by half and the ulcer of the arm was also showing improvement. When last seen in January, 1961, the ulcers were continuing to improve. As the myelomatous process was otherwise asymptomatic neither radiotherapy nor chemotherapy was indicated at that time.

## Discussion.

None of the usual clinical features of multiple myeloma was present in this case, but the diagnosis was suggested by the very high E.S.R., the raised serum globulin and the proteinuria. Large numbers of plasma cells were found on marrow puncture. They were not so abnormal in morphology as myeloma cells often are (Aherne, 1958), but were not considered to be due to chronic infection because the patient had a low serum gamma-globulin. Increased $\alpha_2$-globulin is uncommon in myeloma, but the form of the peak was very suggestive. There was also an abnormal globulin band in the pre-$\beta$ region. Bence-Jones protein was present in the urine.

There were no specific bone changes on x-ray examination but this is not uncommon (Meachan, 1953). It seems likely that the patient had myeloma when first seen in 1959, as the E.S.R. was higher than would be expected in the presence of skin lesions alone and slight proteinuria was found. The ulcers were not the specific lesions of myeloma due to plasma-cell infiltration, but very similar to those reported by Hicks (1950), which may be called "phagedaenic ulcers". Greenbaum (1941), writing about phagedaena geometricum included under this term pyoderma gangrenosum (Brunsting *et al.*, 1930), chronic ulcerative and erosive pyoderma (Tischnenko and Kroiczik, 1928), chronic pyoderma (Ferguson Smith, 1929), chronic undermining and burrowing ulcer (Meleney and Johnson, 1937), phagedaenic ulceration (Holman, 1935), gangrenous impetigo (Meleney, 1933) and postoperative progressive serpiginous ulceration (Cullen, 1924). Greenbaum split them up into those which were primary, occurring as a result of trauma on normal skin and those secondary to operation. The ulceration in Hick's case differed from previous descriptions in two main respects; one was the relative absence of constitutional upset in the patient, and the other was the superficiality of the ulceration. Much attention was paid by the above authors to the bacteriology of the lesions and

little or none to their patients' resistance to infection. However, Brunsting *et al.* (1930), four of whose patients suffered from ulcerative colitis, noted a parallel between the state of the skin ulceration and the concomitant disease.

In multiple myeloma, resistance to infection is lowered and pneumonia is common ; there is also a depression of the immediate and delayed types of allergic reactivity (Bluefarb, 1955). Repeated minor trauma was probably an important factor in initiating and sustaining the ulcers in this case. It seems likely that healing was retarded by a diminished ability to produce gamma-globulin, and therefore antibody, caused by myeloma. Surprisingly, healing was proceeding well when the patient was last seen ; at this stage, he was being treated with oral prednisolone and insufflation of the ulcers with antibiotic powder.

## Summary.

A case is reported of ulceration of the skin occurring in multiple myeloma. In the electrophoretic strip, an intense compact (myeloma-like) band was present in the $\alpha_2$-globulin region with gross reduction of gamma-globulin, but no cryoglobulins were detected. The ulceration might have been a manifestation of diminished resistance to infection due to impaired antibody formation.

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——— and Johnson, B. A. (1937) *Surgery*, **1**, 169.
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# MIGRAINE EQUIVALENT IN THE SKIN.

PORTER F. CRAWFORD, M.D.*

Spartanburg, South Carolina, U.S.A.

Although cutaneous changes have been reported in association with migraine headaches, it is possible that the skin may act as the site of an independent migraine equivalent or variant. This possibility was suggested by unusual recurrent vasomotor changes in a fixed area on a young woman's leg.

## Case Report.

The patient was a 29 year old white woman, the mother of two small children. She stated that she had been having attacks of an eruption every three or four months for the previous four years and that it always appeared in exactly the same area on her leg. She described an attack as consisting of the sudden onset of a rather severe aching pain in the right leg, followed in a few minutes by a warm, bright red discolouration in the same area. This gradually changed over several days' time into a tender black and blue mark. This was visible for about two weeks but between attacks the skin was completely normal.

She stated that only the last three attacks had been attended at their onset by sick headaches. These were identical to ones which she had had occasionally for many years and were described as severe and unilateral. They were preceded by visual symptoms consisting of flashes of bright light and usually lasted about one day. She had no knowledge of similar headaches in members of her family and there was no personal or family history of allergy or epilepsy. Repeated questioning failed to elicit a history of drug ingestion before or of fever with any of the attacks.

An examination of the involved area was made two days after the onset of an attack. Running down the right leg and extending laterally from the anterior edge of the tibia, there was an oval ecchymosis measuring twelve inches by four, moderately well demarcated, bluish red and slightly tender. The lesion was cooler than the surrounding normal skin.

The patient was not seen again but she reported a year later that she had had only one mild attack of the eruption during the interval. This attack was not accompanied by a headache but she had had one independent and severe headache during the year. She attributed her improvement to having had several abscessed teeth extracted.

## Discussion.

A relationship between these skin changes and the migraine symptom complex was suggested by the fact that the changes were recurrent in the same area and were apparently produced by an intense vasodilatation. The patient had migraine headaches and the onset of several of the cutaneous attacks coincided with that of a headache. The fact that several attacks of the skin changes were not accompanied by or associated with headaches suggested that the changes might represent another of the migraine variants or equivalents.

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Other skin changes of a vascular nature have been reported in association with migraine headaches, but they are parts of the symptom complex and are not equivalents capable of appearing independently. For example, a physician who suffered from migraine noted that the seizures were always associated with at attack of Raynaud's phenomenon in his left hand (Briggs, 1958). Redness of the eye on the same side together with flushing of the cheek and forehead are features of the periodic migrainous neuralgia of Wilfred Harris (Bickerstaff, 1959). Actual haemorrhage into the skin of the forehead and eyelid on the side of the headache has been recorded (Selling, 1953).

## Summary.

A case of an unusual eruption possibly representing a cutaneous equivalent of migraine is reported. This is differentiated from others associated with migraine headaches.

## References.

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# SOUTH WEST OF ENGLAND AND WALES SOCIETY OF DERMATOLOGY.

Bristol, February, 1961.

**Multiple Self-Healing Epitheliomata (Ferguson Smith).**—Drs. C. D. Evans and R. P. Warin.

*Case* 1.—A housewife, aged 65.

*History.*—After " bromide poisoning " 30 years ago the first tumour apeared on the cheek and was excised.

Ten years ago she developed a lesion on the left cheek, clinically and histologically giving the appearances of an epithelioma. As this did not respond to radiotherapy it was excised, grafted and a block dissection of the neck carried out.

Eight years ago new lesions on nostril and chin were excised. Dr. A. L. Taylor and Dr. I. Whimster confirmed the histological diagnosis of epithelioma.

Six years ago a tumour on the nostril was excised and 3 years ago one on the left side of the nose was curetted and the histology showed the picture of molluscum sebaceum.

Since this time she has had one more lesion curetted ; 4 others have disappeared spontaneously, but she claims to have " picked " them out.

She has taken no medicines other than a cough mixture in the past, but this did not contain any iodides.

*Family history*—Two brothers. One had similar lesions on the mouth and on the hand : treated respectively with X-rays and excision. He also, at times, developed 3 other lesions which were queried as malignant but apparently resolved spontaneously. A paternal cousin had an epithelioma on the tongue which has remained clear for an 8 year period after treatment with radium needles. The parents and grandparents were from the West Country.

*Examination.*—Scars are present, at sites of treated and untreated lesions.

*Histology.*—Appearances the same as those of benign keratoacanthoma.

*Case* 2.—A male painter and decorator, aged 52.

*History.*—During the past 4–5 years he has developed 10 hard dome-shaped nodules on the face, neck, scalp and right thumb. These have come up in 4–6 weeks, remained stationary for a few weeks and then slowly resolved without any treatment. The resolving lesions become warty in the centre and heal leaving a craggy crater exactly like a benign keratoacanthoma.

*Family history.*—No one else in the family including his 6 brothers has been affected. The paternal grandmother had ichthyosis. Parents and grandparents are Bristolians.

*On examination.*—One new nodule beneath the left lower jaw. Resolving lesions on the back of the neck, over the left angle of the jaw, beneath the right angle of the jaw and on the scalp. Healed pitted scars are visible near the left outer canthus, the left angle of the mouth and on the right cheek and scalp.

*Histology.*—(Dr. Haber). The histology fits in with a clinical diagnosis of Ferguson Smith's self-healing squamous cell epithelioma.

*Comment.*—Histologically and clinically the appearance and behaviour of the tumours in these two cases was exactly like those of benigh keratoacanthoma. In Case 1 other members of the family were affected. It is difficult to know whether these cases should be referred to as recurrent multiple benign keratoacanthoma or multiple self-healing epithelioma (Ferguson Smith). One of the main differentiating points would seem to be the family history in the latter condition and perhaps only Case 1 should come under this diagnosis.

**Nodular Subcutaneous Haemangiomatosis.**—Dr. C. D. Evans.

A man, aged 37.

*History.*—Since childhood nodules have been present under the skin chiefly on the forearms, legs and eyelids. These have gradually become more numerous. There is some discomfort if one is knocked but otherwise there are no symptoms. There are no oral lesions.

*Family history.*—His grandmother and an aunt are similarly affected.

*On examination.*—There are many subcutaneous blue firm nodules on the limbs and face. They feel as if they are thrombosed.

*Investigations.*—Blood count showed 12% eosinophilia and mild neutropenia but no other abnormality. Bleeding and clotting times were normal. Platelets 367,000 per cubic mm. X-rays of chest and skull showed no abnormality.

*Histology.*—Epidermis normal. In the corium are numerous cavernous vascular channels, thin-walled and filled with blood cells, none of which shows any evidence of thrombosis.

*Comment.*—This case appears to be identical with that shown by Goldsmith at the 10th International Congress of Dermatology.

Reference.

Goldsmith, W. N. (1953) *Proceedings of the 10th International Congress of Dermatology.* London: British Medical Association.

Previously reported in *Brit. J. Derm.* (1951) **63**, 153.

**Naevus Acneiformis Unilateralis.**—Dr. L. Tulloch for Dr. C. D. Evans.

A male, aged 19.

*History.*—Two years ago first noticed brown rough raised spots in a line about 2 inches long on the back of the right shoulder. This has increased in length to spread to the back of the right upper arm. Occasionally bleeds with trauma.

*Family history.*—Nil relevant.

*On examination.*—There is a linear lesion 1 cm. wide starting over right scapula and extending to back of right upper arm which is composed of multiple comedones.

*Investigation.*—Histology confirms that this is a typical naevus acneiformis.

*Treatment.*—A small area frozen with liquid oxygen showed some improvement.

**Crossed Epidermal Naevus.**—Dr. L. Tulloch for Dr. R. P. Warin.

A child, aged 2.

*History.*—The condition was present at birth but has become more prominent.

*On examination.*—There are extensive brown velvety patches and bands. These are present over the left side of the scalp, on the face, particularly on the chin and on the right limbs and trunk. The patches stop abruptly at the mid-line on the face and trunk.

No neurological disorder is apparent.

**Colloid Infiltration (Colloid Milia or Colloid Degeneration).**—Dr. R. P. Warin.

A girl, aged 9.

*History.*—The skin was said to be normal until the age of 3 when the condition was first noticed and gradually became worse, but there has been no noticeable progression during the past year. It does not become worse after exposure to sunlight.

*Family history.*—1 sister with no abnormality and 1 brother who had " bumps in scalp " which disappeared when aged 8.

*On examination.*—The eruption is confined to the face and limited by the fringe margin on the forehead, the ears and edge of the chin. It consists of an infiltration

which is diffuse over most of the area but forms papules round the eyelids. She has numerous large freckles which are all depressed (Fig. 1).

*Investigations.*—Urine and faeces showed no excess of porphyrins. Histology (Dr. H. Haber) : Typical colloid infiltration of the skin.

Fig. 1.

*Comment.*—This condition is very uncommon in children, and according to Percival and Duthie (1948) only ten cases had been described up to that time. The relationship to exposure to the sun has been stressed by a number of authors (Zoon *et al.*, 1955; Guin and Everett, 1959). In this case, although not noticeably increased after being in sunshine, the condition is limited by the fringe margin and there is no apparent infiltration beneath the large freckles that she has.

## References.

Guin, J. D. and Everett, R. S. (1959) *Arch. Derm., Chicago*, **80**, 533.
Percival, G. H. and Duthie, D. A. (1948) *Brit. J. Derm.* **60**, 399.
Zoon, J. J., Jansen, L. H., and Hovenkamp, A. (1955) *Ibid.*, **67**, 212.

## ANNOUNCEMENT.

### The International Congress of Dermatology, 1962.

The XIIth International Congress of Dermatology will be held in Washington, D.C., during the period September 9–15, 1962. The Scientific Session, the opening ceremonies, and most of the social activities will be held either at the Park Sheraton or the Shoreham Hotel. Extensive plans for this meeting are in progress. A preliminary information booklet will be mailed to all members of the International League of Dermatological Societies approximately one year before the meeting. Dr. Donald M. Pillsbury of Philadelphia is President of the Congress, and Dr. Clarence S. Livingood of Detroit is the Secretary-General.

Suggestions and questions regarding the Congress are welcomed and should be addressed to the Secretary-General :

Dr. Clarence S. Livingood,
Henry Ford Hospital,
Detroit 2, Michigan, U.S.A.

The general theme of the Congress will be the Application of Advances in Basic Sciences to Clinical Dermatology, to reflect the marked expansion of basic research related to the skin which has occurred during the past decade. A majority of the main papers and introductory discussions will be given by invitation. Three teams of simultaneous translators will function throughout the Congress. Free discussions must be related to the main topics. All applications for places on the programme should be sent with a 150-word abstract to the Chairman of the Scientific Programme Committee, Dr. Donald M. Pillsbury, Duhring Laboratories, University Hospital, 36th and Spruce Streets, Philadelphia 4, Pennsylvania, U.S.A. This may be in any of the four official languages of the Congress (English, French, German and Spanish), but an accompanying English translation, where indicated, will insure accuracy and facilitate prompt consideration. Final arrangements for presentations and formal discussions on the programmes for the various topics will be made upon recommendation of the Chairmen of the respective subcommittees for each topic. Additional periods for Free Communications will be provided insofar as possible.

### Scientific Programme.

*Monday, September* 10 :

Pigmentation (three hours).
Stephen Rothman (Chicago), Chairman.
Consultant, Oscar Gans (Germany).*

* All Consultants are members of the International Committee.

Psoriasis (three hours).
Eugene M. Farber (Palo Alto, California), Chairman.
Consultant, Franjo Kogoj (Yugoslavia).

Methodology of Experimentation, Including Therapeutic Assays (three hours).
Walter B. Shelley (Philadelphia), Chairman.
Consultant, Werner Jadassohn (Switzerland).

*Tuesday, September* 11 :

Cancer (six hours).
Eugene J. Van Scott (Bethesda), Chairman.
Consultants, S. Lapiere (Belgium), Gordon Mitchell-Heggs (England).

Physiology and Physiopathology of the Epidermis (six hours).
William Montagna (Providence), Chairman.
Consultant, Alfred Marchionini (Germany).

Occupational Dermatoses (three hours).
Donald J. Birmingham (Cincinnati), Chairman.
Consultant, S. Lapiere (Belgium).

Mycology (three hours).
J. Walter Wilson (Los Angeles), Chairman.
Consultants, G. B. Dowling (England), Marcial I. Quiroga (Argentina).

*Wednesday, September* 12 :

Radiobiology and Dermatological Radiation Therapy (six hours).
Richard B. Stoughton (Cleveland) Chairman.
Consultant, Guido Miescher (Switzerland).

Systemic Diseases (six hours)
Louis A. Brunsting (Rochester, Minnesota), Chairman.
Consultants, R. Degos (France), Franco Flarer (Italy), Franjo Kogoj (Yugoslavia).

A. Lupus Erythematosus (three hours).
John R. Haserick (Cleveland), Co-chairman.
B. Sarcoidosis (two hours).
Henry E. Michelson (Minneapolis), Co-chairman.
C. Porphyria (one hour).
Louis A. Brunsting (Rochester), Chairman.

Virology (three hours).
Harvey Blank (Miami), Chairman.
Consultant, Alfred Marchionini (Germany).

Colour Television Case Demonstrations and Filmed Case Demonstrations (three hours).
Marion B. Sulzberger (New York), Chairman.
Peter N. Horvath (Washington), Associate Chairman.

*Thursday, September* 13 :

Treponemal Diseases and Non-Treponemal Venereal Diseases, Including Gonorrhoea (six hours).
William J. Brown (Atlanta), Chairman.
Consultant, Sven Hellerström (Sweden).

Acne (three hours).
Walter C. Lobitz, Jr. (Portland, Oregon), Chairman.
Consultant, Marion B. Sulzberger (New York).

Bacteriology (three hours).
Carl T. Nelson (New York), Chairman.
Consultant, Sven Hellerström (Sweden).

Free Communications (three hours).

Live Case Presentations (six hours).
Harry M. Robinson, Jr. (Baltimore), Chairman.
University of Maryland Hospital, Johns Hopkins Hospital, Walter Reed General Hospital.

Colour Television Case Presentations and Filmed Case Presentations (three hours).

*Friday, September* 14 :

Immunology and Allergy (six hours).
Rudolf L. Baer (New York), Chairman.
Consultant, Werner Jadassohn (Switzerland).

Epidemiology of Diseases of the Skin (six hours).
Herman Beerman (Philadelphia), Chairman.
Consultant, Marchial I. Quiroga (Argentina).
WHO Consultants, Jose Gay Prieto (Switzerland), and Alfred N. Bica, (Switzerland).

Systemic Diseases (continued).
D. Dysproteinoses (three hours).
Arthur C. Curtis (Ann Arbor), Co-chairman.
Consultant, R. Degos (France).

Free Communications (three hours).

Colour Television Case Presentations and Filmed Case Presentations (three hours).

# BOOK REVIEWS.

## Lupus*.

This is a study of the epidemiology of lupus and its relationship to other forms of tuberculosis. A nation-wide material was investigated. It consisted of 3902 patients who were admitted to the Finsen Institute from 1895–1954, a figure that is estimated as being 80% of the total incidence of lupus in Denmark. The results of the study are described lucidly and it can fairly be said that all possible information concerning the morbidity of the disease is here related.

During the present century the annual incidence among males is found to have dropped from 25 per million at the turn of the century to 2 per million at the time of completion of the study, and in females from 71 to 4 per million. The fatality ratio, the occurrence in lupus patients of tuberculous disease other than lupus and the relationship of such association with death rate, are among the various aspects of the problem which are gone into fully. The facts appear to show that the presence of lupus in the young is often of more serious significance than many may have supposed.

Owing to the heavy fall in the incidence of lupus, one may suppose that this is likely to be a unique record since no comparable data are ever likely to be available anywhere. A very lengthy and exacting task has been admirably performed and presented. The work ought to be available for reference in all dermatological libraries.

G.B.D.

## Leukaemia.†

Leukemia Cutis is complementary to the author's previous volume on the *Cutaneous Manifestations of the Malignant Lymphomas* and follows a similar pattern. There is a very extensive review of the literature and individual chapters are devoted to the specific manifestations of the various types of leukaemia. Chapters are also devoted to plasmacytic leukaemia (multiple myeloma) and polycythaemia vera.

Non-specific manifestations of all types of leukaemia are grouped together. Much space is devoted to herpes zoster and exfoliative dermatitis and this will be found of considerable interest. The author considers the term leukaemids should be reserved for those lesions of a non-specific character which however show histological changes of a leukaemic nature bringing them into line with the " ids " of syphilis and leprosy. They serve to bridge the gap between specific and non-specific lesions.

This is an authoratative work by a man who has devoted much of his life to the study of his subject and has had access to vast numbers of patients. The bibliography contains over 900 references and it is significant that 13 of these contain Bluefarb as the principal author. The author has done a great service in collecting together and sifting this mass of information. The book is well produced and freely illustrated.

P. D. S.

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* *Lupus Vulgaris* Cutis *in Denmark*, 1895–1954. O. Horwitz. (1960) 142 pp. Price 45s. Also published as Supplement 49 of *Acta tuberc. scand.*

† *Leukemia Cutis*. S. M. Bluefarb (1960). Springfield, Ill. : Charles C. Thomas, Oxford : Blackwell Scientific Publications Ltd. Pp. 489, 169 figs. Price £7 8s.

## Benign Reticuloses.*

A number of controversial subjects is included in this volume notably histiocytoma, juvenile xanthogranuloma, reticulohistiocytoma and granuloma faciale. Not everyone will be pleased with the names chosen to describe these subjects, nor will everyone agree that juvenile xanthogranuloma (naevoxanthoendothelioma) is entirely unrelated to eosinophilic granuloma of bone. Granuloma faciale is the name he uses to describe eosinophilic granuloma of the skin. All these subjects are however fully described by Bluefarb himself and as usual the literature about them is fully reviewed. Other chapters in this work are given to infectious mononucleosis by Bluefarb, lymphogranuloma venereum and cat scratch disease by Orlando Canizares and histoplasmosis by Daniel Kushner.

The book is again well produced and profusely illustrated but there are a few more printers errors than were noted in earlier volumes. Perhaps the printing of a whole line upside-down in the last chapter indicates that the author was less tired at the end of his work than was his proof reader ! All these volumes will undoubtedly be of great value as works of reference. P. D. S.

## Reticuloendothelial Granulomas.†

The present volume is the fourth of a series of monographs concerning the cutaneous manifestations of diseases of the reticulo-endothelial system. In the first two Bluefarb himself described the malignant reticuloses and the leukaemias. The third, dealt with the benign reticuloses. This fourth volume is a composite work with Bluefarb as editor. The first two chapters cover the same ground as Thannhauser's *Lipidoses*. The classification of the diseases concerned is however somewhat different because as Frederick Urbach points out in the first chapter, Thannhauser's classification was based primarily on chemical changes in the blood lipids which, unfortunately, in the light of more recent studies have become less and less well defined.

The first chapter thus covers all the lipoid storage diseases both systemic and localized and includes a very interesting account of lipoid proteinosis. The second chapter written by Bluefarb himself describes the systemic reticuloendothelial granulomas—eosinophilic granuloma, Letterer-Siwe disease, Schüller-Christian disease, etc.

Chapter 3 is a beautifully written account of sarcoidosis by Harold Israel, Herman Beerman and Maurice Sones and the final chapter, which is the longest, is a full account of mastocytosis (urticaria pigmentosa) by Felix Sagher and Zvi Even-Paz. In addition to the various manifestations of the disease itself, they give a full account of the structure and functions of the mast cell which has been the centre of much intensive study during the past twenty years.

This book, like its predecessors, is well produced and profusely illustrated and will prove an invaluable work of reference. It appears that a fifth volume will complete the series and is to be written by Sagher on leprosy. P. D. S.

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* *The Cutaneous Manifestations of the Benign Inflammatory Reticuloses* edited by S. M. Bluefarb (1961). Springfield, Illinois : Charles C. Thomas ; Oxford : Blackwell Scientific Publications. Pp. 408, 85 illus. Price £5 12s. 6d.

† *Cutaneous Manifestations of the Reticuloendothelial Granulomas.* Edited by Samuel M. Bluefarb (1960). Springfield, Ill.: Charles C. Thomas, Oxford : Blackwell Scientific Publications. Pp. 442, 192 illus. Price £5 16*s.* 0*d.*

## The XIth International Congress.*

With the twelfth international congress in Washington approaching, it is appropriate to thank Professor Hellerström, his co-editors and the publishers of the proceedings of the Eleventh International Congress of Dermatology, held in Stockholm. Contributions from all over the world, in four languages but the majority in English, have been brought together in immaculate fashion on high-quality art paper and with first-class reproductions, a truly herculean task.

The first, slim, volume gives an account of ceremonies, organization and entertainments, lists membership and participants, supplies reports of various committees and provides a subject and author index. The second and third volumes comprise six main themes and sixteen symposia with one hundred and forty-eight relevant free communications in addition.

On the theme of biology of skin surface, Spier and Pascher (Munich) contribute a fascinating account of detailed chemical analyses of the water-soluble components of the surface portions of the horny layer. Szakall (Hamburg) provides further information on the water-barrier of the stratum corneum. Warin and Evans (Bristol) had investigated histochemically cases of reticulohistiocytosis and consider that an abnormal polypeptide-lipoid complex is probably present. Ruiter (Groningen) gives a diagram of the localization of vascular changes on the arteriolar tree in arteriolitis allergica cutis. Reviewing occupational dermatoses, Hodgson (Cardiff) succinctly analyses the multiplicity of factors, environmental and personal, relevant in any one case. Pirilä (Helsinki) lists forty-three sensitizers in rubber. The patch tester's lot is obviously not entirely a happy one. New developments in dermatological x-ray therapy allow for discussion of strontium 90 beta-ray applicators and of high-energy electrons (in mycosis fungoides). Cosmetic dermatology forms a main theme and this rapidly growing branch is making a new contribution to the well-being of mankind. Here Belisario (Sydney) gives a characteristically thorough and detailed paper.

The first symposium was on atopic dermatitis. Ingram (described as from London but Leeds and now Newcastle might feel neglected) provides a masterly clinical analysis of Besnier's prurigo. Amongst other applications of antibiotics in dermatology good results of broad-spectrum antibiotics in acne vulgaris and conglobata are reported (Robinson, Jr., Baltimore ; Livingood, Detroit). Discussing barrier creams, Burkhardt (Zurich) finds them useful—with reservations. Bullous dermatoses reveal viewpoints and definitions with a geographical bias but agreement is general on the prime importance of histopathology in diagnosis. Anderson-Roe (Philadelphia) makes a striking contribution. She had rendered skin artifically acantholytic, extracted a fibrous protein, characterized it and suggested that this protein, to be called tonofibrin, might be the keratin precursor forming the fibrillar structure, the tonofilaments of the cellular epidermis.

In their own language (PASpos appears to be the password) the histochemists describe application of their studies to the skin. Photosensitivity always provides a fascinating investigative field. Ouchterlony (Gothenburg) gives an account of diffusion-in-gel techniques when drug allergy is the subject. Bettley and Fairburn (London) used radiosodium clearance studies in evaluating certain cutaneous vascular disorders. Touraine (Paris) classifies ichthyosiform genodermatoses. Venereologists report on newer specific serological tests in syphilis and give long-term results of treatment by penicillin alone. Idse, Guthe and Willcox, (W.H.O., Geneva) review untoward pencillin reactions in treponematoses. Harkness and Haber (London) point out a variant of lichen sclerosus et atrophicus causing stricture of the urinary meatus.

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* *Proceedings of the Eleventh International Congress of Dermatology, Stockholm*, 1957. Edited by S. Hellerström, K. Wikström and A-M. Hellerström. (1959) Lund: Hakar Ohlsson. Vol. I., pp. 90 + xi ; Vol. II., pp. 581 ; Vol. III, pp. 1234.

Relationships of hormones and dermatology provide lively, stimulating papers and allow of reports of successful clinical application of newer synthetic anti-inflammatory hormones. Recent research on fungi, and their classification, finally receive attention.

The above few examples indicate the wide field of valuable information contained in these *Proceedings*. The editors may rest assured that their great contribution to dermatology will always remain appreciated wherever the speciality exists.

M. F.

## Cutaneous Medicine.*

This, a most useful and recommendable book some 430 pages long, is well produced, very fully and excellently illustrated and adequately indexed. When photographs fail to illustrate the authors' meaning they have recourse to well drawn, clear and sometimes humorous diagrams.

The volume contains most things which one would like every medical student to read and every registrar to know. It is not a synopsis of the large work entitled *Dermatology* which the same authors and publishers gave us in 1956, for although much of the subject matter will be found in the larger book this present work has been written afresh.

The authors state that over 80% of patients presenting a skin lesion will have one of forty-five maladies : these can often be diagnosed initially merely by inspection of the patient. It is odd that common varieties of ringworm are omitted from this list. Although the expert will know many other maladies, these include the exotic, the unusual and, often, the insignificant, and, for present purposes, Pillsbury and his colleagues are not interested in them. They therefore concentrate largely on the forty-odd common maladies (including superficial fungus infections), and the exotics (to us) such as yaws, pinta, leishmaniasis and even leprosy are noted only briefly. This may, to some degree, reduce the attractiveness of the book to those who work in the tropics. but those in temperate zones who require a light but accurate, authoritative, up-to-date and readable elementary text-book will be well advised to consider the purchase of this book for their libraries.

R. M. B. McK.

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* *A Manual of Cutaneous Medicine.* D. M. Pillsbury, W. B. Shelley and A. M. Kligman (1961) Philadelphia and London : Saunders. Pp. xii + 430. Price 43*s*. 6*d*.

# CURRENT LITERATURE

**A DEPOT LEPROMIN TEST AND B.C.G. VACCINATION.** J. A. Kinnear Brown and M. M. Stone. (1959) *Lancet*, i, 1260.

The authors describe a method of lepromin testing using the Heaf multi-puncture apparatus. They decided that a 1/100 depot lepromin administered by this method would identify the weak reactors. The late Mitsuda reaction is the one referred to in this paper. Depot lepromin remained in the skin long enough to indicate conversion after subsequent B.C.G. vaccination. Depot lepromin is easier to make and, by this method, to administer. There is considerable economy of material and this may open the way to further investigation of the value of B.C.G. vaccination in protecting children against leprosy. R. H. M.

**SEPARATION OF FACTORS IN LUPUS ERYTHEMATOSUS SERUM REACTING WITH COMPONENTS OF CELL NUCLEI.** H. C. Goodman, J. L. Fahey, R. A. Malmgren and Brecher. (1959) *Lancet*, ii, 382.

Previous studies employing immunological techniques have shown that lupus erythematosus sera may contain several factors reacting with components of cell nuclei. The present report shows that these serum factors can be separated chromatographically into at least two distinct fractions. The evidence further suggests that certain antinuclear activities reside in the 6.6(7) S gamma-globulins (L.E. cell production), and others within the 18 S gamma-macroglobulins. (Authors Summary). R. H. M.

**STRIAE GRAVIDARUM.** L. O. S. Poidevin. (1959) *Lancet*, ii, 436.

In a study of 116 primigravide it was shown that the development of striae did not depend upon skin stretching as measured by increase in girth of abdomen and hips. There is a close relationship between lowered glucose tolerance in late pregnancy and the development of striae, and between acne and breast striae. Other clinical findings suggest an association between striae gravidarum and adrenal cortical hyperactivity. R. H. M.

**ORAL THRUSH IN INFANCY TREATED WITH NYSTATIN.** R. D. Graham. (1959) *Lancet*, ii, 600.

Treatment of infantile thrush by painting the buccal mucosa with gentian violet in 1% aqueous solution was compared with treatment by oral administration of nystatin 100,000 units four times daily. The antibiotic suspension was introduced directly into the child's mouth after feeds. Both groups of patients responded but those treated with nystatin responded more rapidly—within a few days. The author mentions the much greater cost of treatment with nystatin, but does not indicate whether she considers its effect to be due to local or systemic action.
R. H. M.

**HERPETIC WHITLOW.** H. Stern, S. D. Elek, D. M. Anderson and H. F. Anderson. (1959) *Lancet*, ii, 871.

In nurses working in a neurosurgical unit a hitherto unrecognised form of finger infection, due to herpes simplex virus, was found to be common. The lesion can be readily mistaken for a staphylococcal infection, since it becomes secondarily infected with *Staphyloccus pyogenes* ; but it is not associated with trauma, regional adenitis, or constitutional upset. The source was traced to the respiratory secretions of patients : after operation, about 6% excreted herpes simplex virus without any clinical evidence of infection. 49% of the nursing population was found to be susceptible. Herpetic whitlow may be common in hospitals. (Author's Summary).
R. H. M.

**NATURAL HISTORY OF CAVERNOUS HAEMANGIOMATA.** J. R. Simpson. (1959) *Lancet*, ii, 1057.

The changes in 140 untreated cavernous haemangiomata are compared as far as possible with the results in treated cases. Because these lesions almost always resolve spontaneously, more than half disappearing by the age of 5 years, no treatment is recommended. (Author's Summary).
R. H. M.

**PSEUDOXANTHOMA ELASTICUM.** G. M. Berlyne. (1960) *Lancet*, i, 77.

A patient with pseudoxanthoma elasticum presented with gastro-intestinal haemorrhage. The author quotes the view that all patients with gastro-intestinal haemorrhage should be carefully examined for the skin changes of pseudoxanthoma elasticum. When such haemorrhage occurs in this disease, surgical treatment is not indicated. R. H. M.

**ADVANCES IN THE TREATMENT OF SKIN DISEASES.** I. B. Sneddon. (1960) *Practitioner*, **185**, 433.

In the treatment of eczematous eruptions the importance of excluding contact sensitivity reactions is emphasized. The value of topical steroids, often combined with antibiotics or antibacterial agents, is discussed, and in the more chronic eczematous lesions with lichenification the use of occlusive tar bandages is recommended. Careful selection of cases of eczema for treatment with systemic steroids is important.

Exfoliative and erythrodermic psoriasis will respond well to systemic steroids of all types. It is stressed that the most effective treatment of psoriasis at present is the intensive use of ultraviolet light or local applications of tar or dithranol.

Perhaps the most important advances in the management of acne has been the use of small doses of broad-spectrum antibiotics.

Actinic eruptions may be suppressed by the use of antimalarials. These are, however, not without risk.

Although griseofulvin is useful for treating fungal infections it appears that the majority of cases require topical therapy in addition to griseofulvin. R. J. C.

**SOCIAL CASE-WORK IN A DERMATOLOGICAL DEPARTMENT.** M. Brueton. (1960) *Pratitioner*, **185**, 664.

Skin patients may need help from a social worker in order to bring them to terms with their affairs and problems. In attempting the planning of help it is usually necessary to study both aspects of the individual in his environment and his situation. R. J. C.

**THE TREATMENT OF ACNE VULGARIS WITH GRADED ABRASIVE CREAMS.** S. Alexander and H. R. Vickers. (1961) *Practitioner*, **186**, 92.

Seventy-five cases of acne vulgaris of varied severity were treated with graded abrasive pastes for periods of up to nine months. In 25 the condition cleared completely and there was great improvement in a further 37. Only 8 failed to respond. Side effects were minimal.

R. J. C.

**THE CARE OF THE SKIN IN THE NEWBORN.** E. A. Fairburn. (1961) *Practitioner*, **186**, 194.

A practical description of the routine care and a discussion of the commoner conditions including ichthyosis, epidermolysis bullosa, naevi, thermal derangements, infections such as Kaposi's varicelliform eruption, eczema, seborrhoeic dermatitis and napkin rashes. R. J. C.

**A NEW TREATMENT OF LEG ULCERS.** S. D. McAusland. (1961) *Practitioner*, **186**, 227.

Fifty-four cases were treated two to three times daily with oxytetracycline hydrocortisone aersol (Terracortril) and firm bandaging. 43 healed and 11 were improved. This took from two to twelve weeks. R. J. C.

**DERMATITIS DUE TO SYNTHETIC DETERGENTS.** H. S. Samuel. (1961) *Practitioner*, **186**, 485.

The nature and mode of action is described and the incidence of cases of detergent dermatitis discussed. Of 1438 cases recorded 0·9% showed dermatitis due to synthetic detergents. Factors influencing the incidence of detergent dermatitis include the frequency of use of detergents, absence of rinsing of hands, the time and frequency of immersion and the relative humidity of the atmosphere. This latter is considered most important. R. J. C.